Suitable metals for forming the resistive heating element, sensor strip, and bond pads include aluminum, gold, silver, copper, and tungsten.

[0163] The bond pads **40**A and **40**B are connected by electrical leads to the controller, and the controller is preferably programmed to adjust the amount of power supplied to the heating element **34** in dependence upon the resistance of sensor strip **36**. The controller, power source, heating element, and temperature sensor thus form a closed loop temperature control system for controlling the temperature of the chamber **26**. Although a closed loop system is presently preferred, in alternative embodiments the temperature sensor may be eliminated and the chip may be operated in an open loop mode. Further, the processing electronics, including e.g., one or more microprocessors, multiplexers, power control circuitry, and sensor circuitry, may be included in the chip or located externally to the body of the chip and connected thereto.

[0164] The microfluidic chip is preferably used in combination with a cartridge, as previously described with reference to FIG. **2**. One advantage of the flow-through chip is that it allows the analyte from a relatively large volume of fluid sample, e.g. several milliliters or more, to be concentrated into a much smaller volume of elution fluid, e.g., 25 μL or less. In particular, the ratio of the fluid sample volume forced to flow through the device to the volume capacity of the extraction chamber is preferably at least 2:1, and more preferably at least 10:1. In the preferred embodiment, the extraction chamber has a volume capacity in the range of 0.1 to 25 μL, and the volume of fluid sample forced to flow through the device is in the range of 1 to 100 mL, enabling concentration factors of 100 or greater.

[0165] Another advantage of the microfabricated chip is that it allows for rapid and direct heating of the internal attachment surfaces of the chamber. The integral nature and high thermal conductivity of the chamber walls and column structures allow for rapid heat transfer from the heating element directly to the attachment surfaces without necessitating heating of the fluid in the chamber. This improvement inefficiency is significant in terms of the speed, precision, and accuracy of the heating, as well as in the reduction in power required for the heating. In particular, the rapid and direct heating of the internal surfaces to which the analyte is bound greatly increases the degree and efficiency of the elution, and provides a significant improvement over prior art methods and devices.

[0166] A further advantage of the chip is that it includes an array of integrally formed microstructures, preferably high aspect ratio columns, which provide for a high degree of efficiency and control in separating analyte from a fluid sample. In addition to allowing direct and rapid heating of attachment surfaces, the microstructures greatly increase the effective surface area of the chamber which may be used to capture and elute analyte.

[0167] Further, with regularly spaced columns, the diffusion distances between the columns are consistent and there is uniformity of fluid flow so that every analyte is subjected to the same "micro-environment" as opposed to the random nature of beads and fibers. This uniformity allows for predictability of extraction parameters including the time required for each processing step, flow rates, heating amounts, fluid volumes, etc. In addition, the increased efficiency obtained by using an array of internal microstructures and by rapidly and directly heating attachment surfaces allows for the efficient extraction and elution of analytes with relatively high fluid flow rates through the chamber. This decreases the overall time required for the extraction and elution.

[0168] The microfabricated chips of the present invention are also useful for combinatorial synthesis of biopolymers such as oligonucleotides and polypeptides. Combinatorial synthesis allows very large numbers of sequences to be synthesized in a device by transporting, concentrating, and reacting monomers, coupling and deblocking reagents, and catalysts at separately addressable reaction/extraction microstructures. This use exploits the ability of the device to insulate selected microstructures from each other and from nearby reagents.

[0169] The chip **20** may be fabricated using a variety of techniques, including photolithography and/or micromachining. Fabrication is preferably Carried out on silicon or other suitable substrate materials such as glass, silicon dioxide, plastics, or ceramics. A preferred method for fabricating the microfluidic device-using deep reactive ion etching (DRIE) will now be described.

[0170] A 100 mm, n-type (100), 0.1 to 0.2 ohm-cm, double side polished silicon wafer is used as starting material for the base substrate **22**. The wafer thickness it preferably in the range of 350 to 600 μm, depending on the desired structure. In one embodiment of making the chip, an ohmic contact may be made by using phosphorous ion implantation into, a region in the backside, preferably to a depth of 0.2 to 5 μm. Alternatively, a p-type silicon wafer may be used, and the ohmic contact made using boron ion implantation. Implantation is followed by heating of the substrate to activate the dopant.

[0171] The wafer is then spun with photoresist (commercially available from, e.g., Shipley) on the frontside to obtain a photoresist thickness sufficient to mask the DRIE process. This thickness depends upon the final desired depth of the etch. The ratio of silicon etch rate to photoresist erosion rate is typically greater than 50:1. To etch structures that are 200 μm deep, 4 μm of photoresist is usually sufficient. The photoresist is softbaked at 90° C. for about 30 minutes, then exposed with the desired mask pattern, developed, and hardbaked using processes well known in the art of silicon wafer processing.

[0172] FIG. **11** illustrates a sample mask pattern on the frontside of the wafer. The etch mask defines a chamber pattern **44** for forming the extraction chamber in the substrate **22** and an array of column patterns **46** for forming a corresponding array of columns in the substrate. Due to space limitations in drawing size, the etch mask is illustrated with only several hundred column patterns **46**. In the preferred embodiment, however, the array includes 1,000 to 10,000 column patterns for forming a corresponding number of columns in the substrate **22**.

[0173] The patterned wafer is then etched using a DRIE process to form the extraction chamber and integral columns. The DRIE process involves the use of inductively coupled plasma etching and deposition in an alternating fashion, using fluorine based chemistry. Aspect ratios of 20:1 in etched structures are easily realized. The etch rate is typically 2 μm/min or higher.

[0174] After etching, the remaining photoresist is removed from the wafer, e.g., by oxygen plasma etching or wet chemical stripping in sulfuric acid. The substrate is then oxidized to cover the internal surfaces of the chamber, i.e., the chamber walls and surfaces of the columns, with an oxide layer. The oxide layer is preferably 1 to 100 nm thick, and may be